UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,163	11/14/2001	Avi J. Ashkenazi	P2730P1C17	4016

35489 7590 03/31/2006

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,163	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *124-127 and 129-133* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *124,126,127 and 131-133* is/are rejected.

7)☒ Claim(s) *125, 129* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/9/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Part III: Detailed Office Action

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/9/2006 has been entered.

Claims 124-127 and 129-133 are pending and under consideration.

Claims are drawn to PRO1111 protein.

Information Disclosure Statement

The information disclosure statement, filed 1/9/2006, has been considered.

Priority Determination

The utility for the claimed protein is active in a chondrocyte redifferentiation assay. Applicants have established that the PCT application contains the chondrocyte redifferentiation. Accordingly, priority is set at 3/30/00.

Applicants argument that priority is merited to 8/17/1998 has been fully considered but is not deemed persuasive. Applicants argue that the disclosure that PRO1111 has homology to LIG-1 provides utility. This argument has been fully considered but is not deemed persuasive because applicants have not disclosed *what* utility they feel is conferred by that identification.

Applicants have argued in the paper filed 1/9/2006 that priority is merited to at least June 23, 1999 on the basis of gene amplification. This argument has been fully considered but is not deemed persuasive for reasons cited below:

At page 5, applicants reiteratge the argument that amplification of the *gene* encoding the claimed proteins in seven lung tumors and four colon tumors establishes that it is more likely than not that the claimed protein can be used as a cancer diagnostic. This argument has been fully considered but is not deemed persuasive because it is an incomplete and misleading characterization of the data in the specification. According to the specification at page 552-553, seven of nineteen lung tumor cell lines and four of seventeen colon tumor cell lines tested positive. However, it remains that the amplification was minimal, and that the most parsimonious explanation is aneuploidy, with no evidence that the chromosome bearing PRO1111 was preferentially amplified (as opposed to other chromosomes). Aneuploidy is also a feature of damaged tissue, and is commonly found in colon and lung tissues, which are subject to environmental damage. It does not invariably or inevitably lead to cancer; rather, such damaged cells are generally removed by the body via apoptosis; the development of cancer is the exception, as evidenced by the fact that the general population is constantly suffering damage to lung cells via air pollution, whereas lung cancer remains relatively rare. Further, it remains that the 2-3 fold amplification of the nucleic acid is consistent with a simple case of aneuploidy, in which there is a single extra copy of the chromosome in question, and is *not* predictive of a similar differential in protein expression; hence, the argument is not persuasive, as the claims are drawn to polypeptides, not the nucleic acids that encode them. Merely because amplification *may* be an *initial* step in the formation of cancer does not equate with a substantial assertion of diagnostic utility for the encoded protein. There is no factual support for applicant's assertion at the bottom of page 5 of the response that "it helps in identifying individuals at *significantly increased cancer risk" (*emphasis added).

The Declaration by Dr. Goddard has been fully considered but is not deemed persuasive. In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed.

Cir. 1993). Affidavits or declarations are provided as evidence and must set forth facts, not merely conclusions. In re Pike and Morris, 84 USPQ 235 (CCPA 1949).

It is noted that the declaration is one originally filed in application number 09/903925, and is dated 1/16/2003. Declarant discusses the accuracy of the Taq DNA polymerase assay, stating that the Taqman PCR technique is sensitive enough to detect at least a 2-fold increase in gene copy number (paragraph 3) and that this increase is significant and useful. This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO1111gene has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. The specification merely demonstrates that the PRO1111 *nucleic acid* was amplified in some cancers, to a minor degree (about 2-3 fold). No mutation or translocation of PRO1111 has been associated with any type of cancer versus normal tissue. It is not known whether PRO1111 is expressed in corresponding normal tissues, and what the relative levels of expression are. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1111 is amplified in a variety of samples, including some normal tissues, and invites the artisan to determine the significance of this increase. One cannot determine from the data in the specification whether the observed "amplification" is associated with any change in protein expression, nor whether the protein was expressed in *any of the tissues at all.* It remains that, as evidenced by Pennica et al., the issue is simply not predictable, and the specification presents a mere invitation to experiment.

Furthermore, the Declaration does not provide data such that the examiner can independently draw conclusions. Only Doctor Goddard's conclusions are provided in the declaration. It is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, as discussed above, Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column) and discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a

strong and significant correlation between expression level and a published role in the disease (see discussion section).

Applicants argument of the Pennica reference at page 8 of the response has been fully considered but is not deemed persuasive. Applicants have plucked a single phrase from the portion cited by the Examiner, which phrase supports their assertion of utility. However, they have taken that phrase out of context; the teachings of Pennica as a whole support the opposite conclusion, that utility of the polypeptide cannot be predicted based upon amplification of the nucleic acid, for reasons set forth at page 5 of the office action mailed 7/6/2004.

Applicant argues at pages 11-12 that the Examiner has improperly generalized the teachings of Pennica and Konopka. This argument has been fully considered but is not deemed persuasive because both references are cited to establish the state of the art, which is that it is not predictable that a protein will be significantly amplified based upon a minor amplification of the nucleic acid encoding it. It is necessary to cite specific examples to form a general argument.

At pages 8-9, applicants argue that the Haynes reference establishes a general trend, and that few data points deviated from the expected, and thus that Haynes shows that the data meet a "more likely than not" standard of predictability. This argument has been fully considered but is not deemed persuasive because Figure 1 of Haynes, argued by applicants, shows data correlating *protein and mRNA* levels, not genomic DNA levels and protein. Applicants have not provided any mRNA data for PRO1111. Only DNA levels are provided, no mRNA or protein levels. Accordingly, the data in the specification as filed cannot be correlated with those of Haynes. Further, the figure clearly has a tight cluster of data points showing little or not protein expression at the region corresponding to 2-3 copies of mRNA. However, the principle for which Haynes was originally cited by the Examiner still applies: Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (p. 1863, second paragraph, and Figure 1). That is Haynes' conclusion, not the Examiner's. The 'general trend' pointed to by applicants is seen at a level of mRNA copy number that has not been established for PRO1111, nor is it predictable from the observation of 2-3 copies of *DNA* per cell.

It is noted that all the references cited by the Examiner appeared in peer-reviewed publications. Applicants repeatedly try to impugn the statistical methods used therein, by general allegation. The Examiner finds no merit in this argument.

Applicants arguments pertaining to the Ornoft, Hyman and Pollack references remains not persuasive for reasons of record. Ornoft et al. *could only compare the levels of about 40 well-resolved and focused abundant proteins."* (See abstract.) It would appear that applicants have provided no fact or evidence concerning a correlation between such low levels of amplification of DNA, found only in a minority of tested tumors which were not characterized on the basis of those in the Ornoft publication, and an associated rise in level of the encoded protein. The Hyman reference cited by applicants found 44% of *highly* amplified genes showing overexpression at the mRNA level, and 10.5% of highly overexpressed genes being amplified; thus, even at the level of high amplification and high overexpression, the two do not correlate. Further, the article at page 6244 states that of the 12,000 transcripts analyzed, a set of 270 was identified in which overexpression was attributable to gene amplification. This proportion is approximately 2%; the Examiner maintains that 2% does not provide a reasonable expectation that the slight amplification of SEQ ID NO: 228 would be correlated with elevated levels of mRNA, much less the claimed protein. Further, Hyman does not examine protein expression. Applicants are reminded that the instant claims are directed to proteins. Similarly, Pollack, cited by applicants, does not analyze protein levels, nor does Pollack support the assertion that it is predictable, on the basis of the minimal increase in copy number of SEQ ID NO: 228 that the protein would accordingly be found at altered levels. Accordingly, it remains that the significance of the gene amplification data is questionable, and cannot be predictably extrapolated as applying to the claimed protein. The art, taken as a whole, clearly teaches that it is not predictable that a two-fold copy increase in the nucleic acid would translate to detectable over-expression of the associated mRNA, much less any protein encoded thereby. Further, as evidenced by the Ornoft publication, the type of data presented in the instant specification clearly does not meet the standard in the art for establishing association of a protein with cancer.

The Polakis declaration was fully considered in the previous Office Action. No further comment is necessary.

It remains that the art considers that that gene amplification does not reliably correlate with polypeptide over-expression, and thus the level of polypeptide expression must be tested empirically. The instant specification does not provide this additional information, and thus the skilled artisan would need to perform additional experiments. Since the asserted utility for the claimed polypeptides is not in currently available form, the asserted utility is not substantial. Applicants arguments to the contrary fail to meet the urged "more likely than not" standard, but rather fall well within the category that significant further experimentation would be required to determine if the claimed polypeptides have the urged utility, experimentation of the type that was found to be impermissible by the court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct,.1966).

The effective priority date remains set at 3/30/2000.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 132-133 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NO: 229 or fragments of such that are usable for making antibodies or have chondrocyte redifferentiation activity, does not reasonably provide enablement for proteins that are encoded by a nucleic acid that is amplified in adenocarcinomas or squamous cell carcinomas of the lung or in adenocarcinomas of the colon. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims for reasons of record in the previous Office Action.

Applicants argue that one could go find additional embodiments without undue experimentation. This argument has been fully considered but is not deemed persuasive because it has not been established that the protein of SEQ ID NO: 229 is a diagnostic, much less that

there are variants of it that are diagnostic. The recitation of the term "native sequence" is both indefinite and lacks adequate written description. It remains that applicants have found a single nucleic acid, SEQ ID NO: 228, that is found to be aneuploid in a small number of tumor cell lines; there is no enablement that the encoded protein is enabled, nor that there are variants of the protein within the metes and bounds of the claims.

There are no working examples of proteins less than 100% identical SEQ ID NO:229. There is but one function potentially attributed to PRO1111 that meets the requirements of 35 U.S.C. §112, first paragraph: stimulation of chondrocyte redifferentiation. While the specification generally describes properties of cytokines, it is acknowledged that cytokines are diverse in function and structure. The specification does not provide guidance for using polypeptides related to (*i.e.,* 80%-99% identity) but not identical to SEQ ID NO:229 which do not have the single specific disclosed activity potentially shown for PRO1111. The claims are broad because they do not require the claimed nucleic acid to encode a polypeptide identical to the disclosed sequence and because the claims have no functional limitation.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of proteins and lack of knowledge about function(s) of encompassed polypeptides structurally related to SEQ ID NO:229, the potential one limited working example of PRO1111 polypeptide and its one function, the lack of direction or guidance for using polypeptides that are not identical to SEQ ID NO:229, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claims 124, 126-127 and 130-133 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification teaches that PRO1111 has (unspecified) homology to proteins having leucine rich repeats, for example see pages 19 and 353. The structure of the putative PRO1111 peptide is disclosed as comprising two putative transmembrane domains at page 147 of the

specification; however, it is clear from the disclosure that (a) only one of the two, if any, is likely to actually *be* a transmembrane domain, (b) there is no conception of whether the protein is a type I or type II transmembrane protein, or (c) if it *is* a transmembrane protein, which end of the protein would be the 'extracellular' domain. Claims 132-133 do not require that the claimed protein possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. The other claims have been amended to require chondrocyte redifferentiation function. Therefore, claims specifically to the extracellular domain lack adequate written description.

Further, claims 132-133 are newly amended to recite that the polypeptide is of a "native sequence". There is written description of a single species only, SEQ ID NO: 229. There is no written description or conception of any other "native sequences".

Applicants traversal that the recitation of a functional property in the claims overcomes the rejection. It is noted that the recitation "the nucleic acid encoding said polypeptide is amplified in adenocarcinomas or squamous cell carcinomas of the lung or in adenocarcinomas of the colon" is not a functional recitation *per se,* but rather a descriptor of where one might encounter the nucleic acids that encode the claimed protein. This argument has been fully considered but is not deemed persuasive because applicants have not established that there is any conception of nucleic acids in a manner commensurate in scope with the claims, and hence of the claimed polypeptides. All applicants have presented is a single nucleic acid found to be slightly amplified in a small proportion of cancers, and the germ of an idea that there might be variants of the nucleic acid that would be similarly associated. There is no evidence of the actual conception of such nucleic acids, nor is there any evidence of record that they exist. Hence, there is accordingly no written description of the claimed polypeptides, other than the one identified as SEQ ID NO: 229. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Accordingly, the rejection is maintained.

Applicants arguments of enablement, that it would not require undue experimentation to determine if other species within the metes and bounds of the claims exist, is not pertinent to this rejection, which is on the grounds of lack of adequate written description. It remains that the

specification discloses a single nucleic acid that encodes a single protein; there is no specific conception of how nature might alter either, which is what applicants now seek to claim.

Therefore, proteins comprising the sequence set forth in SEQ ID NO: 229 or active or antigenic fragments thereof but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 132-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of "native sequence polypeptide having at least 95% sequence identity", as recited in claim 32, cannot be determined, as the specification discloses only the protein of SEQ ID NO: 229, and not all naturally occurring proteins that are 95% identical to such (or 99%). The Examiner interprets "native sequence" to mean "naturally occurring". Without adequate written description of such, one of ordinary skill in the art would not be able to determine whether a given protein met or did not meet the limitations of the claims. As no naturally occurring sequences having 95 or 99% identity to SEQ ID NO: 229 are described, the metes and bounds of claims 132-133 cannot be determined. It cannot be determined which 90% identical sequences are or are not native sequences. Were one handed a protein in a test tube, one could not determine whether or not that protein was within the metes and bounds of claim 1. Without a description of all naturally occurring proteins within the metes and bounds of the claim, a given isolated protein cannot be ascribed as being either naturally occurring or not naturally occurring. Accordingly, the claim is indefinite. Once a protein is made, it is not

possible to determine how it was made, nor its original source (it is noted that the claim encompasses naturally occurring proteins that have been synthesized recombinantly or chemically, as well as those isolated from nature). The sequence and structural properties in no way reveal the origin of the molecule or its forebears.

Rejections Over Prior Art:

Priority is set 3/30/00.

A search of the nucleic acid sequence databases revealed the following prior art:

Reference	Date	Author	Identity to SEQ ID NO:228
AI769814	12/21/99	NCI-CGAP	100% to bases 1703-2180
AI435407	3/30/99	NCI-CGAP	99.8% to bases 1743-2185
AI470931	4/13/99	NCI-CGAP	100% to bases 1795-2179
T15752	7/25/96	R. Berry et al.	100% to bases 1870-2184
U.S. Patent Number 6,689,866, SEQ ID NO: 9	3/8/00	Shimkets	99.7% to bases 1-2183
U.S. Patent Number 6,689,866, SEQ ID NO: 31	3/8/00	Shimkets	Encodes XC domain, 100% identity to SEQ ID NO : 229, residues 45-492.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 124-127, 129 and 132-133 remain rejected under 35 U.S.C. 102(a) as being anticipated by Wang et al., Genbank Accession No. AF196976, cited by applicants. The sequence of Wang et al. differs from that of SEQ ID NO: 128 by only a single nucleotide, according to applicants alignment. The sequence is described as encoding "Homo sapiens tumor associated protein NAG14". The single nucleotide change is silent, that is, both sequences encode a Valine residue at that position. Cleavage of the signal sequence would automatically occur when expressing the protein in a mammalian cell. Accordingly, the claims are anticipated by Wang et al.

Claims 119-123 and 132-133 are rejected under 35 U.S.C. 102(a) as being anticipated by Jacobs et al., Genbank Accession No. AAY28806, cited by applicants. The sequence of Jacobs et al. differs from that of SEQ ID NO: 129 by only a single amino acid, according to applicants alignment. Accordingly, the claims are anticipated by Jacobs et al. Applicants arguments

regarding the priority date of the application have been fully considered but are not deemed persuasive for reasons cited above with respect to the priority determination.

Claims 130-133 remain rejected under 35 U.S.C. 102(a) as being anticipated by Jacobs, WO 99/50405. SEQ ID NO: 2 of the publication is 99.7% identical to SEQ ID NO: 229 of the instant application. Fusion proteins, including to epitope tags, are disclosed at page 54. The reference is silent with respect to whether or not the nucleic acid encodes a protein with chondrocyte redifferentiation activity. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Applicants arguments regarding the priority date of the application have been fully considered but are not deemed persuasive for reasons cited above with respect to the priority determination.

Claims 124, 127, and 130-133 remain rejected under 35 U.S.C. 102(e) as being anticipated by Shimkets, U.S. Patent Number 6,689,866 or US Patent Application Publication US2003/0054514 A1, or US Patent Application Publication US2003/0003532 A1. The US Patent Application Publications are divisionals of the patent, and differ only in the claims. The '514 publication contains claims to nucleic acids, proteins (see claim 11), and antibodies (see claim 13), and the '532 application contains claims to nucleic acids and vectors. The teachings will be discussed with reference to the issued patent. SEQ ID NO: 9 of the patent is 99.7% identical to SEQ ID NO: 228 of the instant application, at bases 1-2183 (bases 159-2341 of the patent), and encodes a protein 99.2% identical to that of SEQ ID NO: 229. SEQ ID NO: 31 is a fragment of SEQ ID NO: 9, is identified as encoding the extracellular domain (see figures 17A

and 17B), which is 100% identical to residues 45-495 of SEQ ID NO: 229. Fusion proteins, including Ig fusions, are disclosed beginning at column 32, line 50.

Accordingly, the claims are anticipated by Shimkets.

Applicants arguments regarding the priority date of the application have been fully considered but are not deemed persuasive for reasons cited above with respect to the priority determination.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 130 and 132-133 remain rejected under 35 U.S.C. 103(a) as being obvious over any one of Loci AI769814, AI435407 , AI470931, or T15752, in view of Sibson et al. For reasons of record in the previous Office action.

The teachings of the primary references are summarized in the Table above. Each has over 99% identity to SEQ ID NO: 228 over the full length of the locus from the database. As

sequence identity is calculated relative to the shorter of the two sequences being compared, the proteins encoded by the sequences would meet the limitations of claims 130-132.

Sibson et al. disclose that it is generally useful to place a desired cDNA sequence into an expression vector, host cell, and express the encoded protein, as well as to raise antibodies to proteins encoded by such cDNA's. See pages 8-13. Fusion proteins are disclosed at page 8 as being useful for purification of the encoded protein.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the DNA's disclosed by any one of the primary references to express and then isolate the encoded polypeptide as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above.

Applicants argument that ESTs are not enabling disclosures since they provide no utility has been fully considered but is not deemed persuasive. Utility as defined by 35 U.S.C. §101 is not required for a finding of obviousness. The EST disclosures disclose and enable one of ordinary skill in the art to make the DNAs disclosed therein. Sibson provides the motivation to express such sequences. Accordingly, the invention as claimed is *prima facie* obvious. Applicants arguments regarding the priority date of the application have been fully considered but are not deemed persuasive for reasons cited above with respect to the priority determination.

Claim 131 remains rejected over any one of Loci AI769814, AI435407 , AI470931, or T15752, in view of Sibson et al. and further in view of Capon et al., U.S. Patent Number 5,116,964 for reasons of record in the previous Office action. Applicants have presented no further argument of this rejection.

Claims 130 and 131 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al., Genbank Accession No. AF196976, cited by applicants, in view of Capon et al., U.S. Patent Number 5,116,964 for reasons of record in the previous Office action for reasons cited with respect to claim 131 in the rejection over one of Loci AI769814, AI435407 ,

AI470931, or T15752, in view of Sibson et al. and further in view of Capon et al., U.S. Patent Number 5,116,964 in the previous Office Action.

Advisory Information:

Claims 125 and 129 remain objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Ms. Brenda Brumback, at telephone number 571-272-0961.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to 571-273-8300. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner